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(FILE 'HOME' ENTERED AT 14:45:59 ON 15 JUL 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
AT 14:46:22 ON 15 JUL 2003

L1 1852 S TRANSGENIC (L) (CHICKEN OR HEN OR FOWL OR BIRD)
L2 72 S L1 AND (INTERFERON OR ERYTHROPOIETIN OR EPO OR IFN)
L3 39 DUP REM L2 (33 DUPLICATES REMOVED)
L4 17 S L3 AND PY<=1997
L5 17 SORT L4 PY

FILE 'STNGUIDE' ENTERED AT 14:52:25 ON 15 JUL 2003

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
AT 14:54:01 ON 15 JUL 2003

E IVARIE ROBERT?/AU
L6 21 S E2
L7 3 S L6 AND TRANSGEN?
L8 3 DUP REM L7 (0 DUPLICATES REMOVED)
L9 6 S L6 AND TRANS?
L10 29 S E1
L11 17 S L10 AND TRANS?
L12 5 S L11 AND EGG?

=> d an ti so au ab pi l12 1-5

L12 ANSWER 1 OF 5 MEDLINE
AN 2002719100 MEDLINE
TI Avian **transgenesis**: progress towards the promise.
SO TRENDS IN BIOTECHNOLOGY, (2003 Jan) 21 (1) 14-9. Ref: 76
Journal code: 8310903. ISSN: 0167-7799.
AU Ivarie Robert
AB The hen has long held promise as a low cost, high-yield bioreactor for the production of human biopharmaceuticals in **egg** whites. A typical **egg** white contains 3.5-4.0 grams of protein, more than half of which comes from a single gene (ovalbumin). Harnessing the power of the gene to express a recombinant protein could yield up to a gram or more of the protein in the naturally sterile **egg**. Accordingly, a major effort has been underway for more than a decade to develop robust methods for modification of the chicken genome. This effort intensified in the mid-1990s when several avian **transgenic** companies entered the scene. Progress has been made in that time but much remains to be done.

L12 ANSWER 2 OF 5 MEDLINE
AN 2002190519 MEDLINE
TI Expression of exogenous protein in the **egg** white of **transgenic** chickens.
SO NATURE BIOTECHNOLOGY, (2002 Apr) 20 (4) 396-9.
Journal code: 9604648. ISSN: 1087-0156.
AU Harvey Alex J; Speksnijder Gordon; Baugh Larry R; Morris Julie A;
Ivarie Robert
AB Using a replication-deficient retroviral vector based on the avian leukosis virus (ALV), we inserted into the chicken genome a **transgene** encoding a secreted protein, beta-lactamase, under the control of the ubiquitous cytomegalovirus (CMV) promoter. Biologically active beta-lactamase was secreted into the serum and **egg** white of four generations of **transgenic** chickens. The expression levels were similar in successive generations, and expression levels in the magnum of the oviduct were constant over at least 16 months in **transgenic** hens, indicating that the **transgene** was stable and not subject to silencing. These results support the potential of the hen as a bioreactor for the production of commercially valuable, biologically active proteins in **egg** white.

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 2002:931060 CAPLUS
DN 138:215789
TI Avian **transgenesis**: progress towards the promise
SO Trends in Biotechnology (2002), Volume Date 2003, 21(1), 14-19

CODEN: TRBIDM; ISSN: 0167-7799

AU **Ivarie, Robert**

AB A review. The hen has long held promise as a low cost, high-yield bioreactor for the prodn. of human biopharmaceuticals in **egg** whites. A typical **egg** white contains 3.5-4.0 g of protein, more than half of which comes from a single gene (ovalbumin). Harnessing the power of the gene to express a recombinant protein could yield up to a gram or more of the protein in the naturally sterile **egg**. Accordingly, a major effort has been underway for more than a decade to develop robust methods for modification of the chicken genome. This effort intensified in the mid-1990s when several avian **transgenic** companies entered the scene. Progress has been made in that time but much remains to be done.

L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS

AN 2002:291304 CAPLUS

DN 137:135738

TI Expression of exogenous protein in the **egg** white of **transgenic** chickens

SO Nature Biotechnology (2002), 20(4), 396-399

CODEN: NABIF9; ISSN: 1087-0156

AU Harvey, Alex J.; Speksnijder, Gordon; Baugh, Larry R.; Morris, Julie A.; **Ivarie, Robert**

AB Using a replication-deficient retroviral vector based on the avian leukosis virus (ALV), the authors inserted into the chicken genome a **transgene** encoding a secreted protein, .beta.-lactamase, under the control of the ubiquitous cytomegalovirus (CMV) promoter. Biol. active .beta.-lactamase was secreted into the serum and **egg** white of four generations of **transgenic** chickens. The expression levels were similar in successive generations, and expression levels in the magnum of the oviduct were const. over at least 16 mo in **transgenic** hens, indicating that the **transgene** was stable and not subject to silencing. These results support the potential of the hen as a bioreactor for the prodn. of com. valuable, biol. active proteins in **egg** white.

L12 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS

AN 2000:145005 CAPLUS

DN 132:204036

TI Direct avian oviduct **transgenesis** for exogenous protein expression in poultry **eggs**

SO PCT Int. Appl., 54 pp.

CODEN: PIXXD2

IN **Ivarie, Robert**; Harvey, Alex J.; Murphy, George F., Jr.; Rapp, Jeffrey C.

AB Methods for prepg. **transgenic** avians which express exogenous protein substantially only in their oviducts are disclosed. Each of the methods comprises delivering nucleic acid expression cassettes directly to the oviducts of the avians. The exogenous protein expressed by the expression cassette is secreted into the lumen of the avian oviduct and secreted into the **eggs** of the **transgenic** avians. Methods for prepg. **eggs** which contain exogenous protein, such as human interferon, and methods for the prodn. of proteins are also disclosed. The methods for direct oviduct **transgenesis** may also be used to assess the suitability of expression cassettes or exogenous proteins for expression in the avian oviduct.

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

| | | | | |
|------------------|----|----------|-----------------|----------|
| PI WO 2000011151 | A2 | 20000302 | WO 1999-US19393 | 19990825 |
| WO 2000011151 | A3 | 20000615 | | |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|------------|----|----------|---------------|----------|
| AU 9956907 | A1 | 20000314 | AU 1999-56907 | 19990825 |
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L3 39 DUP REM L2 (33 DUPLICATES REMOVED)
L4 17 S L3 AND PY<=1997
L5 17 SORT L4 PY

FILE 'STNGUIDE' ENTERED AT 14:52:25 ON 15 JUL 2003

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AT 14:54:01 ON 15 JUL 2003

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L5 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2003 ACS
AN 1995:645229 CAPLUS
DN 123:49258
TI Chicken **interferon** gene, its sequence and recombinant
expression, and its antiviral action
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
IN Sekellick, Margaret J.; Marcus, Philip I.; Ferrandino, Anthony F.
AB A **chicken interferon** gene sequence and its deduced
amino acid sequence is provided. There is also disclosed a method of
producing biol. active **chicken interferon**
recombinantly, a method of isolating other non-mammalian
interferon genes, a method of making a **transgenic**
fowl having the **chicken interferon** gene
incorporated therein, and a method for delivery of the **chicken**
interferon in the **bird**, such as by genetic immunization
or aerosol. Expression of the gene yields functional **chicken**
interferon. Thus, **chicken interferon** cDNA was
isolated which coded for the complete mature **interferon** sequence
of 162 amino acids plus a 31-residue signal peptide. A cDNA probe was
also isolated, consisting of 269 nucleotides with a 5'-primer region of 32
bases, a 3' primer region of 20 bases, and a 217-base partial sequence of
the **chicken interferon** gene. The probe can be used in
screening a non-mammalian cDNA library by std. procedures. Glycosylated
recombinant **chicken interferon** could be expressed in
transfected mouse L(Y) cells, human WISH cells, and COS-1 cells, and
displayed antiviral activity. **Chicken interferon** cDNA
can be integrated into plasmid or retroviral vectors under the control of
the **chicken** metallothionein promoter (for Cd or Zn induction)
and introduced into sperm, egg, or zygote of **fowls** in order to
prevent viral and/or parasitic infection.

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 9511302 | A1 | 19950427 | WO 1994-US11660 | 19941021 <-- |
| W: AU, BR, CA, JP, KR | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5641656 | A | 19970624 | US 1993-139909 | 19931022 <-- |
| US 5885567 | A | 19990323 | US 1994-308821 | 19940919 |
| AU 9480771 | A1 | 19950508 | AU 1994-80771 | 19941021 <-- |
| AU 684849 | B2 | 19980108 | | |
| EP 724638 | A1 | 19960807 | EP 1994-931841 | 19941021 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL | | | | |

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E IVARIE ROBERT?/AU
L6 21 S E2
L7 3 S L6 AND TRANSGEN?
L8 3 DUP REM L7 (0 DUPLICATES REMOVED)

=> d an ti so au ab pi l8 2

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 1999:271485 CAPLUS
DN 130:277660
TI Vectors comprising a magnum-specific promoter for avian
transgenesis
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
IN Ivarie, Robert D.; Harvey, Alex J.; Morris, Julie A.; Liu,
Guodong

AB This invention provides vectors and methods for the stable introduction of
exogenous nucleic acid sequences into the genome of a bird and for
expressing said exogenous sequences to alter the phenotype of the bird or
to produce desired proteins. In particular, **transgenic** chickens
are produced which express exogenous sequences in their oviducts. Eggs
which contain exogenous proteins are also produced. In one specific
embodiment, an avian leukosis virus retroviral vector is used which
comprises a modified pNLB plasmid contg. an exogenous gene that is
inserted downstream of a segment of the ovalbumin promoter region. The
total length of the ovalbumin promoter segment may be from about 0.88 kb
to about 7.4 kb in length, and includes both the steroid-dependent
regulatory element and the neg. regulatory element. An RNA copy of the
modified retroviral vector, packaged into viral particles is used to
infect embryonic blastoderms which develop into **transgenic**
birds. Alternatively, helper cells which produce the retroviral
transducing particles are delivered to the embryonic blastoderm.

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 9919472 | A1 | 19990422 | WO 1998-US21975 | 19981015 |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2307840 | AA | 19990422 | CA 1998-2307840 | 19981015 |
| AU 9911899 | A1 | 19990503 | AU 1999-11899 | 19981015 |
| AU 752946 | B2 | 20021003 | | |
| EP 1023442 | A1 | 20000802 | EP 1998-954994 | 19981015 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | |
| JP 2001520009 | T2 | 20011030 | JP 2000-516025 | 19981015 |

| L Number | Hits | Search Text | DB | Time stamp |
|----------|------|--|---|------------------|
| 1 | 1695 | Transgenic WITH (chicken OR bird or fowl or turkey or hen) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/15 14:20 |
| 7 | 661 | ((Transgenic WITH (chicken OR bird or fowl or turkey or hen)) and egg | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/15 14:12 |
| 13 | 16 | ((Transgenic WITH (chicken OR bird or fowl or turkey or hen)) and egg) and (egg SAME interferon) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/15 14:13 |
| 19 | 7 | ((Transgenic WITH (chicken OR bird or fowl or turkey or hen)) and egg) and (egg SAME erythropoietin) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/15 14:13 |
| 25 | 21 | ((Transgenic WITH (chicken OR bird or fowl or turkey or hen)) and egg) and (egg SAME interferon)) or (((Transgenic WITH (chicken OR bird or fowl or turkey or hen)) and egg) and (egg SAME erythropoietin)) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/15 14:13 |
| 31 | 28 | Transgenic WITH (chicken OR bird or fowl or turkey or hen).clm. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/15 14:20 |
| 38 | 16 | (US-6395961-\$ or US-6333192-\$ or US-6156569-\$ or US-5897998-\$ or US-5784992-\$ or US-5162215-\$ or US-H001065-\$ or US-4997763-\$ or US-6515199-\$).did. or (US-20020116732-\$ or US-20020108132-\$ or US-20020028488-\$ or US-20010039668-\$ or US-20030126629-\$ or US-20030126628-\$ or US-20030074681-\$).did. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/15 14:29 |
| 41 | 16 | ((US-6395961-\$ or US-6333192-\$ or US-6156569-\$ or US-5897998-\$ or US-5784992-\$ or US-5162215-\$ or US-H001065-\$ or US-4997763-\$ or US-6515199-\$).did. or (US-20020116732-\$ or US-20020108132-\$ or US-20020028488-\$ or US-20010039668-\$ or US-20030126629-\$ or US-20030126628-\$ or US-20030074681-\$).did.) and stage | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/15 14:29 |
| - | 4905 | 800/\$?.ccls. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:07 |
| - | 835 | 800/\$?.ccls. and (chick\$10 or bird or fowl) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:25 |
| - | 34 | (800/\$?.ccls. and (chick\$10 or bird or fowl)) and (transgen\$10 ADJ (chick\$10 or bird or fowl)) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:08 |
| - | 12 | (US-4997763-\$ or US-H001065-\$ or US-5162215-\$ or US-5897998-\$ or US-6156569-\$ or US-6333192-\$ or US-6395961-\$ or US-5784992-\$).did. or (US-20010039668-\$ or US-20020028488-\$ or US-20020108132-\$ or US-20020116732-\$).did. | USPAT; US-PGPUB | 2002/09/16 13:21 |
| - | 2 | ((US-4997763-\$ or US-H001065-\$ or US-5162215-\$ or US-5897998-\$ or US-6156569-\$ or US-6333192-\$ or US-6395961-\$ or US-5784992-\$).did. or (US-20010039668-\$ or US-20020028488-\$ or US-20020108132-\$ or US-20020116732-\$).did.) and (EPO or interferon\$10) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:25 |

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|---|------|---|---|------------------|
| - | 51 | (800/\$?.ccls. and (chick\$10 or bird or fowl)) and EPO | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:27 |
| - | 1213 | EPO and (chick\$10 or bird or fowl) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:26 |
| - | 486 | (EPO and (chick\$10 or bird or fowl)) and transgenic\$10 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:26 |
| - | 31 | (800/\$?.ccls. and (chick\$10 or bird or fowl)) and Erythropoietin\$5 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:34 |
| - | 110 | (800/\$?.ccls. and (chick\$10 or bird or fowl)) and interferon\$5 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:42 |
| - | 300 | (800/\$?.ccls. and (chick\$10 or bird or fowl)) and egg\$2 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:42 |
| - | 65 | ((800/\$?.ccls. and (chick\$10 or bird or fowl)) and egg\$2) and (interferon or erythropoietin) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/09/16 13:43 |